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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/623,705 | 09/07/00 | BJORSNE | M 3525-95 |

HM12/0814

NIXON & VANDERHYE
1100 NORTH GLEBE ROAD 8TH FLOOR
ARLINGTON VA 22201-4714

| EXAMINER | |
|---|---|
| ROBINSON, B | |
| **ART UNIT** | **PAPER NUMBER** |
| 1625 | 7 |

**DATE MAILED:** 08/14/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/623,705 | BJORSNE ET AL. | |
| | Examiner | Art Unit | |
| | Binta M. Robinson | 1625 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-26 is/are pending in the application.

4a) Of the above claim(s) 2 and 21-26 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 and 3-20 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

The examiner notes the applicant's election of Example 2 at paper no. 8. The election of species will be used as a reference point for the examiner to create a natural genus based on a liberal interpretation of the doctrine of legal and chemical equivalence and restriction will be required under 35 U.S.C. 121 and 372.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in response to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1 and 3-20, drawn to the compound of formula I where A is a single bond, C1-6 is alkylene, -O(CH2)m-, m is 0-4, R4 is H or C1-6 alkyl, R5a, R5b, R5d, R5e, Rf are H or C1-3 alkyl, R2 and R3 are H, C1-4 alkyl (Optionally substituted with CN), OR7 where R7 is H, C1-6 alkyl or –(CH2)b-aryl where aryl is carbocyclic, b is 0-4, D is H, C1-4 alkyl, -OR9, where R9 is H, C1-6 alkyl, X is O or S, and R1 is C1-12 alkyl, a pharmaceutical composition, a method of treatment of an arrhythmia with a compound of formula I, and a process for the preparation of a compound of formula I.

Group II, claim(s) 1-20, drawn to the compound of formula I, a pharmaceutical composition, a method of treatment of an arrhythmia with a compound of formula I, and a process for the preparation of a compound of formula I.

Group III, claim 21 drawn to a compound of formula II

Group IV, claim 22 drawn to a compound of formula IV

Group V, claim 23 drawn to a compound of formula VIII

Group VI, claim 24 drawn to a compound of formula XX

Group VII, claim 25 drawn to a compound of XXII

Group VIII, claim 26 drawn to a process for the preparation of a compound of formula VIII, XX, XXII or XXXV

The inventions listed as Groups I-VIII do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The species lack a common core.

By virtue of the applicant's election of species which falls into Group I genus, Group I will be examined. Claim 2 and the unelected portions of claims 1, 3-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

If applicant files a divisional application on the subject matter in group II or group VIII, the subject matter in groups II or VIII may be subject to further restriction.

1. Applicant is advised that should claim 1 be found allowable, claim 15 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

2. Applicant is advised that should claim 1 be found allowable, claim 16 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1 and 3-20 in part are rejected under 35 U.S.C. 112, first paragraph, because the specification, while providing enablement for heterocyclic rings morpholinyl, purinyl, benzimidazolyl, pyrimidinyl, piperazinyl, pyrazinyl, piperidinyl, pyridinyl, pyrrolinyl, pyrrolidinyl, pyrrolidinonyl, triazolyl, imidazolyl, quinolinyl, isoquinolinyl, dioxanyl, benzodioxanyl, benzodioxolyl, benzodioxepanyl,

benzomorpholinyl, indolyl, pyrazolyl, pyrrolyl, benzothiophenyl, thiophenyl, chromanyl, thiochromanyl, benzofuranyl, pyranyl, tetrahydropyranyl, tetrahydrofuranyl, furanyl, the specification does not reasonably provide enablement for Het1, Het2, or Het3 equal to all five to ten-membered heterocyclic rings containing one or more heteroatoms selected from oxygen, nitrogen and/or sulfur, and which also optionally includes one or more =O substituents in lines 13- 15 of claim 1 on page 72 and all other occurrences throughout claims 1 and 3-20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement. The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. The applicant is referred to ***In re Wands***, 858 f.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in ***Ex parte*** Foreman 230 USPQ 546 (Bd. Of App. And Inter 1986).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1)the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art 6) the amount of direction provided by the inventor 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In

re Wands, 858 F. 2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

5. Claims 1 and 3-20 in part are rejected under 35 U.S.C. 112, first paragraph, because the specification, while providing enablement for phenyl or napthyl on lines 1-3 on page 7 of the specification, does not reasonably provide enablement for all aryl groups in lines 4 of claim 1 on page 72 and all other occurrences throughout claims 1 and 3-20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims as recited are broader than the scope of enablement. The specification lacks direction or guidance for placing all of the alleged products in the possession of the public without inviting more than routine experimentation. The applicant is referred to ***In re Wands***, 858 f.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) which includes the incorporation of the 8 factors recited in ***Ex parte*** Foreman 230 USPQ 546 (Bd. Of App. And Inter 1986).

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6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim(s) 11, 13, 14, 20 in part are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 20 in part, the term "derivative" is indefinite. It is unclear as to compounds are being claimed.

B. In claims 13 and 14, the phrase "an effective amount of the compound to a patient in need thereof" is not included in these pharmaceutical claims. Pharmaceutical claims should include references to "an effective amount" of a compound being administered to a host in need thereof.

C. In claim 1, lines 4-6, page 72, and all other occurrences in claims 3-20, the phrase "(all of which are optionally substituted and/or terminated (as appropriate) by one or more substituents selected from OH, halo, cyano, nitro, C1-4 alkyl and/or C1-4 alkoxy)" is vague and ambiguous. How can R1 be terminated by more than one terminating group, if a terminating group, by definition, should terminate a radical? The phrase "(as appropriate)" in line 5, page 72 of claim 1 is also vague and ambiguous.

D. In claim 1, lines 22-23, page 74, and all other occurrences throughout claims 3-20, the phrase "(in which latter three groups" is indefinite. The phrase "A represents a single bond, C1-6 alkylene... -OH groups);" between lines 21-24 on page 74, should be rewritten in the form " A is ___, ___ or ____, or ___, ___, ___, and ___ which are optionally substituted with A and B, or ___ and ____ which are attached to the bispidine nitrogen..."

E. In claim 11, line 3, page 60, the phrase "in which latter two cases p is 1, 2, or 3)" is indefinite. The term "wherein" is suggested.

F. In claim 19, lines 3-4, page 61, the phrase "to a person suffering from, or susceptible to, such a condition" is indefinite. The phrase "to a patient in need thereof" is suggested.

G. In claims 17 and 18, line 1, the term "use" is indefinite because it is not statutory language.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 3-20 are rejected under 35 U.S.C. 103(a) as being unpatentable Lubisch et. al. . (See Reference N, EP 0308843).

Lubisch et. al. teaches the instant compound as shown in Formula I, where R is halogen, C1-C4 alkoxy, R1 is Halogen, C1-C4 alkoxy, Z is C1-C4 alkylene, R3 is H, C1-C4 alkyl, and R5 is C1-C4 alkyl. At page 5, rightmost column, lines 30-35, see formula I. The difference between the prior art compound and the instantly claimed compounds is the teaching of a generic compound versus a disclosed species. It would have been obvious to one of ordinary skill in the art to select various known radicals within a genus to prepare structurally similar compounds. Accordingly, the compounds are deemed

unpatentable therefrom in the absence of a showing of unexpected results for the claimed compounds over those of the generic prior art compounds.

8. The elected species appears to be allowable.

9. The IDS filed 2/20/2001 has been considered.

10. The EP 0308848 A2 reference cited as an X reference on the international search report appears to be an X reference

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (703) 306-5437. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Alan Rotman can be reached on (703)308-4698. The fax phone numbers for the organization where this application or proceeding is assigned are (703)308-7922 for regular communications and (703)308-7922 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703)308-0193.

Binta M. Robinson
August 12, 2001

D. MARGARET SEAMAN
PRIMARY EXAMINER